RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-23 were originally filed with the application. Claims 24-26 were added. Claims 13 and 19-23 were withdrawn from consideration as directed to a non-elected invention. Claim 1 is currently amended. Support for this amendment can be found in claims 5-7 and 9 as originally filed, and in the Specification, for instance at page 5, lines 1-27; page 6, lines 3-31; and page 12, line 3, to page 13, line 15. No new matter has been added. Claims 1-12, 14-18, and 24-26 are submitted herein for reconsideration.

B. Rejections Under 35 U.S.C. §103

The Action rejects claims 1-12, 14-18, and 24-26 as obvious over Heim *et al.* (U.S. Patent Application Publication No. 2003/0188345A1, filed June 28, 2001), in view of Lange *et al.* (U.S. Patent No. 5,939,539) and Ebinuma *et al.* 1997 (*Proc. Natl. Acad. Sc*i USA 94:2117-2121). Specifically, the Action states that Heim *et al.* disclose use of a plant cell non-lethal negative selectable marker (*codA*) in vector backbone DNA for combined positive/negative selection, Lange *et al.* teach a plant hormone degradative/modifying gene as a selectable marker, and Ebinuma *et al.* teach use of the isopentenyl transferase gene (*ipt*) as a selectable marker. Thus it is asserted that it would have been *prima facie* obvious for one skill in the art to modify the teachings of Heim *et al.* with those of Lange *et al.* and Ebinuma *et al.* Applicants respectfully traverse.

Applicants initially note that claim 1 has been amended, and that the obviousness rejection is moot in view of this. Applicants also submit that the claims are not rendered obvious by Heim *et al.* in view of Lange *et al.* and Ebinuma *et al*, in that Heim *et al.* do not teach a plant

cell non-lethal negative selectable marker gene within the meaning of the claims, and neither Lange nor Ebinuma cure this defect. *codA* is described at paragraphs 23 and 25 of Heim as a marker gene that may be used in a combined positive/negative selective scheme as described by Gallego *et al.* (*Plant Mol. Biol.* 39:83-93, 1999). However, Gallego describes *codA* as a lethal marker gene, *i.e.* conferring sensitivity to added 5-fluorocytosine (5-FC). More specifically, *codA* may be described as a conditional lethal marker gene, in that its lethal effect requires the presence of the added 5-FC, as noted in the present Specification, for instance at page 3, lines 13-20, and at page 30, lines 10-16, while in the absence of 5-FC *codA* does not function as a marker gene.

The Action asserts that it would have been *prima facie* obvious to modify the teachings of Heim to use other negative selectable marker genes such as those taught by Lange or Ebinuma, since Heim motivates one of skill in the art "to use other selectable markers, including non-lethal negative selectable markers" [Action, page 5, 1st paragraph]. However, nowhere does Heim discuss use of a non-lethal negative selectable marker gene. The terms "lethal" or "non-lethal" are not found in Heim. The term "selectable" is not found in Heim. The term "marker" is found throughout Heim, however, it is only used in the context of lethal or conditional lethal markers. There is no motivation for one of skill in the art to combine these references. Applicants thus respectfully submit that this assertion that Heim motivates the use of any non-lethal selectable markers, let alone "other" non-lethal selectable markers, is unsupported, and represents hindsight reasoning. A *prima facie* case of obviousness has therefore not been established.

Further, even if the references were properly combined, the addition of the cited Lange and Ebinuma references does not cure the defect in Heim. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.

M.P.E.P. § 2143.03; *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). As noted previously, Lange does not describe use of gibberellin 20-oxidase (GA 20 oxidase) as a selectable marker, including as a non-lethal selectable marker. Rather, use of the GA20 oxidase is in the context of its effect on agronomic or horticultural characteristics. The present Action does not address the arguments put forth in this regard in the previous response.

Regarding Ebinuma *et al.* Applicants note that (loss of) an already present *ipt* gene is being used as a screenable marker, and not as a non-lethal negative selectable marker. Applicants submit that some confusion regarding the term "selection" may have arisen. As typically used in the art, a "selectable" marker is distinguished from a "screenable" marker, *e.g.* in that in the first instance the presence or absence of the marker interferes with the ability of a cell or organism to develop or survive and is thus, under certain conditions or at some developmental stage, biochemically or genetically lethal. In contrast, screenable markers allow for development of a cell or organism, while providing a phenotype that distinguishes cells possessing the marker from those which do not, such as a visible phenotype. A skilled worker may then "select" (*i.e.* more properly screen for or score) a cell or organism based on this phenotype, but this sense of the term is clearly distinct in the art from its use in the first instance. Thus, these terms are used differently by the Action (*e.g.* when the Action at page 6, 1st full paragraph, states that Ebinuma combined with Heim teach that the *ipt* gene produces a "selectable phenotype") and by Ebinuma, as compared with their use in the present Specification, and in the claims as read in view of the Specification. Applicants respectfully submit that Ebinuma is describing a screenable phenotype, and the only "selection" is occurring is at the hands of the experimenter.

Applicants further note that Ebinuma teaches away from use of *ipt* as a selectable marker gene (*i.e.* as in the first instance above), by noting that transgenic plants possessing the *ipt* gene are unable to regenerate normally (*i.e.* to develop roots). Instead, Ebinuma describes use of a system wherein loss of the *ipt* marker, via *Ac* transposition and deletion, is detectable (*i.e.* screenable or scorable), but is not being genetically or biochemically "selected" as the term "selected" is used in the present Specification.

Applicants also respectfully submit that, in spite of the Action's unsupported assertion that the "Applicants' recitation 'non-lethal negative selectable marker gene' is read as an intended use of a selection marker gene" [Action, page 6, end of 1st full paragraph], these different types of marker genes are functionally distinct, as is outlined in the present Specification, for instance at page 3, line 7, wherein it is noted that plant cells containing the non-lethal selectable marker gene are potentially rescuable. The present claims thus recite distinct DNA constructs in view of the above, and the Action's characterization of *codA,* GA20, and *ipt* as "non-lethal negative selectable markers" is inaccurate and does not agree with the use of the term in the Specification, cited references, or the understanding of one of skill in the art.

Applicants also respectfully submit that the described unexpected result, that is the effect of the presence of a non-lethal negative selectable marker gene in inhibiting regeneration of transgenic plants that contain backbone sequences, is commensurate with the scope of the present claims. The Specification teaches multiple examples of non-lethal negative selectable marker genes for use with the claimed DNA constructs. The Action acknowledges these results as they relate to marker genes involved in modifying plant hormone levels, which would include hormone synthesis, substrate diversion, or degradation as presently claimed (*e.g.* Action, page 7). Regarding metabolic interference marker genes, Applicants respectfully submit that the

Specification, for instance at page 4, lines 6-30, and page 17, lines 5-25, describes several genes that may interfere with plant metabolism and with regeneration and growth of transgenic plants, and the effects of these genes on plant and plant cell growth is known. Thus, the unexpected result detailed in the Specification, for instance at page 35, lines 15-28, and in the previous response, whereby the percentage of plants lacking backbone sequences is substantially increased, is commensurate with the claims.

In light of all the above, Applicants respectfully request that the rejection under 35 U.S.C. §103 be withdrawn.

C. Conclusion

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned at (214) 259-0932 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

/Ron J. Laby/

Ron J. Laby
Reg. No. 53,173
Agent for Applicants

Sonnenschein Nath & Rosenthal, L.L.P.
1717 Main Street, Suite 3400
Dallas, Texas 75201
(214) 259-0900

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